Induction of pluripotent stem cells by small RNA-guided transcriptional activation

Grant Award Details

Induction of pluripotent stem cells by small RNA-guided transcriptional activation

Grant Type: New Cell Lines

Grant Number: RL1-00660

Project Objective: The goal of this project is to develop a new methodology for reprogramming cells by finding small activating RNAs (saRNA) that can induce each of the reprogramming factors, thereby replacing the need for retroviral transfection.

Investigator:

Name:	Long-cheng Li
Institution:	University of California, San Francisco
Type:	PI

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: $1,368,461

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4 (NCE)

View Report

Grant Application Details

Application Title: Induction of pluripotent stem cells by small RNA-guided transcriptional activation

Public Abstract: Embryonic stem cells have great potential in therapeutic use to replace diseased or damaged tissues because they have the unique capability of giving rise to any cell type of the body while perpetuating their own identity, even after repeated cell divisions. Recent advances in this area have resulted in a new way to generate stem cells from specialized adult cells by introducing 3 to 4 genes encoding proteins called stem cell factors, which are highly active in natural stem cells, into these adult cells using viruses as the carrier. These derivatives are called induced pluripotent stem (iPS) cells and have properties that are very similar to those of embryonic stem cells. Because iPS cells can be generated from the patient's own tissues, problems associated with immune rejection are avoided. Furthermore, this process does not use embryos, so there are no ethical concerns. Unfortunately, the use of viruses to generate these cells is problematic because the virus may also activate harmful genes in the cells, such as those that cause cancer. We recently developed a way to switch on inactive genes in human cells using small RNA molecules instead of viruses, and coined the technique "RNAa" for RNA-induced gene activation. We have shown that RNAa can induce robust and prolonged activation of a variety of genes. RNAa therefore seems well suited to replace virus-mediated reprogramming as a means to generate iPS cells. The main goal of this application is to develop a novel method of transforming adult cells into stem cells without using viruses. Accomplishment of our study will bring iPS cells one step closer to the clinical application of stem cell therapy.

Statement of Benefit to California: The aim of this application is to develop new approaches for the generation of pluripotent stem cell lines without using virus as the gene expression vector. Stem cells so generated can be used to replace diseased or damaged tissues without the concern of virus-related adverse effects such as insertional mutagenesis. Success of these approaches will benefit the health of the population and the economy of the State of California. Californians suffer many diseases and injuries that are treatable by using stem cells, such as Parkinson's and Alzheimer's disease, diabetes and cancer. The new stem cell lines and reagents we generate will likely be commercialized by California-based biotechnology companies and thus generate revenue and new job opportunities for the state.